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Analysis of long-COVID symptoms and COVID-19 complications

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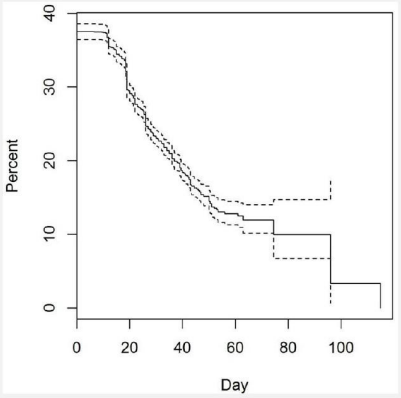
[DateTime]

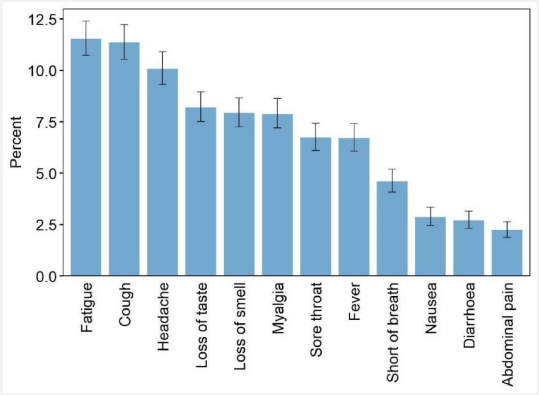
1 in 5 respondents have symptoms at 5 weeks

- Percentage with any symptom = 21.0% at 5 weeks from infection; 9.9% at 12 weeks
- Median duration among those with symptoms = 39.5 days

Day-by-day percentage with any symptom



Percentage with symptoms at 5 weeks, by symptom



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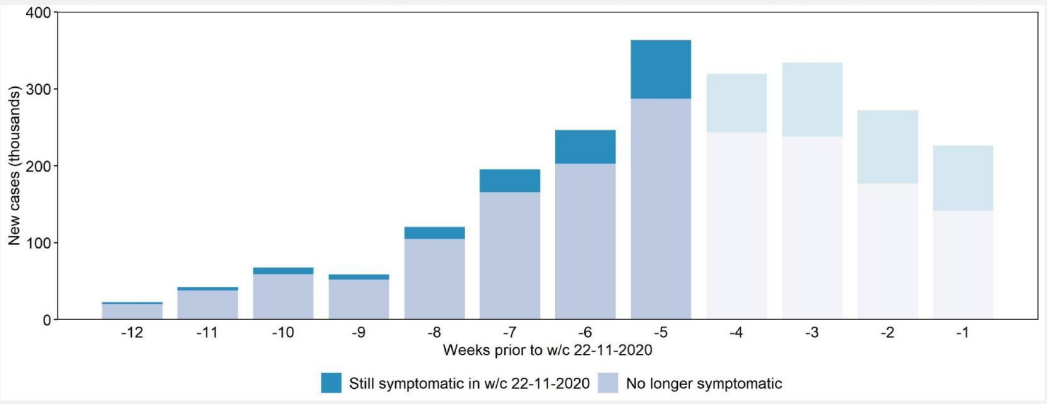
- Source: ONS Coronavirus Infection Survey data to 07-12-2020
- Unweighted sample of 8,193 respondents who tested positive for COVID-19 during follow-up
- Symptoms at or within 5 weeks of infection are tracked until first observed discontinuation
- Symptom probabilities and durations obtained from Kaplan-Meier estimation

Estimated number of people in England with symptoms lasting 5-12 weeks in w/c 22-11-2020:

186,000 (95% CI: 153,000 - 221,000)

Estimated incidence of COVID-19 in England, broken down by whether still symptomatic at 22-11-2020



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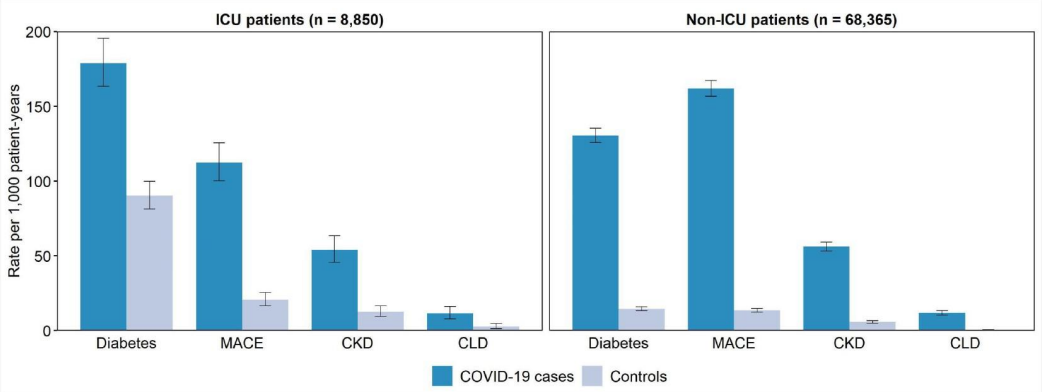
- Estimates represent only people in private households; communal establishments are excluded
- Incidence counts sourced from ONS, Coronavirus Infection Survey, UK: 11 December 2020
- *K*-week symptom probabilities obtained by Kaplan-Meier estimation
- Approximate 95% CI estimated by simulation with 10,000 replications, reflecting uncertainty in both incidence counts and symptom probabilities

COVID-19 hospitalisation is associated with increased risk of adverse events

Rates of adverse events among hospitalised COVID-19 patients compared with matched controls



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- Sources: HES to Aug 2020, GPES to Sep 2020, death registrations to Sep 2020
- Diabetes includes both type 1 and type 2; MACE: major adverse cardiovascular event (a composite of heart failure, myocardial infarction, stroke and arrhythmia); CKD: chronic kidney disease stages 3-5, including dialysis and kidney transplant; CLD: chronic liver disease
- Matching variables: age, sex, ethnicity, region, IMD quintile, smoking status, pre-existing conditions (hypertension, MACE, respiratory disease, CKD, CLD, diabetes, cancer)

Next steps for linked data study

- Analytical improvements:
  - Only consider diagnoses following COVID-19 discharge
  - Time-to-event analysis accounting for competing risk of death
  - Stratification of estimates by age, sex, ethnicity and IMD quintile

- Enhanced data sources:
  - More recent data, including the “second wave”
  - New long-COVID primary care codes
  - Linked national testing data for those not hospitalised
  - Linked demographic and socio-economic characteristics from the Census

Appendices

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Background

Our research focusses on two broad categories of outcomes:

1. Long-COVID symptoms

- Experimental estimates using data from COVID-19 Infection Survey (CIS)
- Time-to-cure for symptoms developing within 5 weeks of infection
- Work in progress – new long-COVID question in early 2021

2. COVID-19 complications

- Initially focussing on hospitalised patients (ICU and non-ICU)
- Linked GP, hospital and death records
- COVID-19 patients matched to controls on demographic and clinical profiles
- Assessed rates of CVD, CKD, liver disease, diabetes

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Limitations of long-COVID symptoms study

Limitation of analysis	Consequence	Direction of impact on prevalence
Estimates are unweighted	Not fully representative of population	Unknown
Does not account for differential loss-to-follow-up	Experience of some respondents, e.g. older people, may be truncated	Downwards
Assumes continuous symptoms	Relapse not taken into account	Downwards
Long-COVID defined from week 5 rather than week 4	People with post-acute symptoms who were infected 4 weeks ago not captured	Downwards
Symptoms estimated up to maximum duration of 12 weeks	People with symptoms lasting more than 12 weeks not captured	Downwards
Covers only subset of symptoms reported by long-COVID sufferers	Some symptoms (e.g. cognitive impairment) not captured	Downwards
No data on severity of symptoms	Impact on day-to-day activity is unknown	Upwards

New long-COVID question on CIS – early 2021

Would you describe yourself as having "long COVID", that is, you are still experiencing symptoms more than 4 weeks after you first had COVID-19, that are not explained by something else? ☐ Yes ☐ No

If yes: (a) Does this reduce your ability to carry-out day-to-day activities compared with the time before you had COVID-19? *(select one)* ☐ Yes, a lot ☐ Yes, a little ☐ Not at all

(b) Have you had any of the following symptoms as part of your experience of long COVID? Please include any pre-existing symptoms which long COVID has made worse (answer Yes or No for each one)

Fever	☐ Yes ☐ No	Headache	☐ Yes ☐ No	Muscle ache	☐ Yes ☐ No
Weakness/tiredness	☐ Yes ☐ No	Nausea/vomiting	☐ Yes ☐ No	Abdominal pain	☐ Yes ☐ No
Diarrhoea	☐ Yes ☐ No	Loss of appetite	☐ Yes ☐ No	Loss of taste	☐ Yes ☐ No
Loss of smell	☐ Yes ☐ No	Sore throat	☐ Yes ☐ No	Cough	☐ Yes ☐ No
Shortness of breath	☐ Yes ☐ No	Chest pain	☐ Yes ☐ No	Palpitations	☐ Yes ☐ No
Vertigo/dizziness	☐ Yes ☐ No	Anxiety/worry	☐ Yes ☐ No	Low mood	☐ Yes ☐ No
Trouble sleeping	☐ Yes ☐ No	Memory loss or confusion	☐ Yes ☐ No	Difficultly concentrating	☐ Yes ☐ No

COVID-19 patients are atypical of the wider population

Selected baseline summary statistics for COVID-19 patients compared to the broader patient population

Characteristic	Category	Patient population sample (n = 200,000)	ICU COVID-19 patients (n = 10,065)	Non-ICU COVID-19 patients (n = 76,890)
Age	<30 years	3.2%	3.2%	2.9%***
	30-49 years	34.1%	17.7%***	10.7%***
	50-69 years	54.7%	53.3%**	24.8%***
	70+ years	6.6%	22.4%***	60.0%***
IMD quintile	1 (most deprived)	19.7%	24.5%***	24.9%***
	5 (least deprived)	19.0%	14.7%***	15.1%***
BMI	≥30 kg/m^2 (obese)	21.9%	36.9%***	26.3%***
Any previous hospital admission		58.3%	72.2%***	87.3%***
Comorbidities	Hypertension	23.1%	46.1%***	60.4%***
	MACE	6.1%	13.0%***	34.9%***
	Respiratory disease	15.0%	28.4%***	49.3%***
	CKD stage 3+	2.8%	8.8%***	19.6%***
	Liver disease	1.7%	4.2%***	5.8%***
	Diabetes	9.6%	29.6%***	30.0%***
	Cancer	9.6%	16.8%***	25.7%***

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Matching variables for linked data study

Demographics

- Age (<50 years, 50-69 years, ≥70 years)
- Sex (male, female)
- Ethnicity (White, Black, Asian, Mixed/Other, unknown)
- Region (North, South, Midlands, unknown)
- IMD quintile (1-5, unknown)

Risk factors

- Smoking status (current, former, never/unknown)
- BMI (unknown or <25 kg/m^2, 25 to <30 kg/m^2, ≥30 kg/m^2)

Pre-existing conditions (based on diagnoses 2010-19)

- Hypertension
- Major adverse cardiovascular event (MACE) (composite of heart failure, stroke, MI and arrhythmia)
- Respiratory disease
- Chronic kidney disease (CKD) stage 3+ (including dialysis and kidney transplant)
- Chronic liver disease (CLD)
- Diabetes mellitus (both type 1 and type 2)
- Cancer

Limitations of the linked data study

- Survivorship bias – only see outcomes for those who survived acute phase of infection (likely to be those in relatively better health)
- Outcomes in control group may not fully reflect background risk due to reduced health services contact among the vulnerable
- Matching is unlikely to fully balance differences in risk profile – recent hospitalisation (for any cause) may indicate more severe impairment
- Severity thresholds for hospitalisation are not constant through time and space